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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/606,230	06/26/2003	Yoshitake Yamamoto	D-1205CIP	4227

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EXAMINER	
TURK, NEIL N	

ART UNIT	PAPER NUMBER
1743	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/606,230	YAMAMOTO, YOSHITAKE	
	Examiner	Art Unit	
	Neil Turk	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *June 25th, 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date. _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Remarks

This Office Action fully acknowledges Applicants remarks made on June 25th, 2007. Claims 1 and 3-7 are pending. Claim 7 is newly added.

Priority

The disclosure of the prior-filed application, Application No. 10/015,668, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The 10/015,668 application does not provide adequate support or enablement for the subject matter of claim 6. The 10/015,668 disclosure for spectrometry conditions is drawn to positive and negative ion detection modes and not to molecular ion detection and fragment ion detection modes. Thereby, claim 6 will not receive the filing date of the prior-field application, 10/015,668, filed on 12/17/2001.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the elements necessary to perform the various mass spectrometry conditions and obtaining of spectrum and chromatogram data. Claim 1 recites a chromatogram mass spectrometer for sequentially processing a sample,

however the body of the claim only recites the various control/operational elements. Claim 1 lacks the necessary elements for such control operations to perform their recited functions. It appears that claim 2 brings in the structural elements of the chromatogram mass spectrometer for carrying out the operations claimed in claim 1.

Claims 1 and 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 generally recites a setting device, spectrometry execution device, and an operation device. However, Applicant's drawings and specification recite a control portion 21, signal process portion 20, and operating portion 22. From Applicant's pre-grant publication (2004/0126277) the setting device as currently claimed appears it could be drawn to both the operating portion 22 and/or the control portion 21. Paragraph 0037 states that an operator inputs various parameters through the operating portion 22 such as an operating condition of LC or of the MS portion, and a process condition in the signal process portion 20. Paragraph 0039 states that when the spectrometry starts the control portion 21 first sets parameters of the respective portions of MS portion for the molecular ion detection mode, and carries out the mass scan. Further, from this description it appears the spectrometry execution device as currently claimed could be drawn to either the operating portion or the control portion. The operation device as claimed generally recites that it adds spectrum intensities. Paragraphs 0040 and 0041 discuss the signal process portion 20 in which it processes the detection signals changing sequentially, and obtains the mass spectrum data which is then added to obtain the chromatograph data A(0) and A(1). Paragraph 0042 recites that A(0) and A(1) are added

together to obtain chromatogram data A and it is outputted as an analogue value, but does not recite which structure of the device carries out such a process. Claim 1 should be corrected so as to clearly match up the recited setting device, spectrometry execution device, and operation device with those structures discussed and shown in Applicant's specification.

It is also unclear in claim 1 how the adding of data is being done and which data is added together. Figure 3 shows the flowchart which shows that chromatogram data A(0) comes from the molecular ion detection mode and the mass spectrum data, and A(1) comes from the fragment ion detection mode and the mass spectrum data, and finally that data A is the addition of A(0) and A(1). The language as currently recited is unclear with respect to the disclosure and figures as pertain to the adding of the data.

Claim 1 is unclear in where the chromatograph portion lies structurally in the device, such that the specification only recites a column 4 of the LC (paragraphs 0031-0032, fig. 2). It is unclear if this column 4 of the LC is the same as the chromatograph portion that is being claimed.

Claim 3 recites a fraction control device as a further structure to the chromatograph mass spectrometer. However, paragraph 0032 recites that the control portion 21 controls operations of the respective portions in the MS portion, the fraction collector, and the respective portions of the LC. There does not appear to be a separate fraction control device, as this seems to be a further limitation within the capability/functionality of the control portion 21.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-5, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP06102251A (translated Derwent Abstract Acc. No. 1994-161274), hereafter JP, in view of Stevens (4,762,617).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Stevens teaches a chromatogram system with two detectors and a fraction collector (Fig. 1). Chromatogram data are added or subtracted to scale the data (lines 56-58, col. 4).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by the positive and negative ionization detection in order to scale data in a two-detection scheme chromatograph such as taught by Stevens. It would have been obvious to modify the JP device to include a fraction collector to collect desired fractions as taught by Stevens, under control of the detector signal as was known in the art.

Claims 1, 3-5, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP in view of Windig (6,329,652).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Windig teaches a method for data handling for an LC-MS system. A summation of particular data is plotted to obtain an enhanced chromatogram (lines 1-19, col. 4).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by the positive and/or negative ionization detection in order to enhance chromatograms such as taught by Windig. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1, 3-5, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP in view of Watanabe (6,444,979).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Watanabe teaches a method for data handling for a chromatogram-MS system. A summation of particular data is plotted to obtain a chromatogram of all mass vs. time (columns 7 and 8, figs. 4-7a).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by positive and/or negative ionization detection in order to provide a cumulative chromatogram as taught by Watanabe. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1, 3-5, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP in view of Sacks (5,205,845).

JP teaches a liquid chromatograph coupled to a mass spectrometer with a controller for alternatively or, under program control, providing either positive or negative ion detection mode. JP further teaches that the ionization mode is switched by the switching of a valve and then the ionization is performed in the opposite ionization mode (different ionization modes).

JP does not disclose an operation device for adding data.

Sacks teaches a method for data handling for a chromatographic system. A summation of particular data of the multiple columns forms a single chromatogram from FID 16, and in this way the chromatographic time dimension can be used more efficiently (lines 9-47, col. 8).

It would have been obvious to modify the JP device to add the data from the chromatograms generated by the positive and/or negative ionization detection in order to provide a single chromatogram and thus allow the chromatogram time dimension to be used more efficiently such as taught by Sacks. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1 and 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman et al. (A Novel Precursor Ion Discovery Method on a Hybrid-Quadrupole Orthogonal Acceleration Time-of-Flight (Q-TOF) Mass Spectrometer for Studying Protein Phosphorylation, 2002, American Society for Mass Spectrometry), hereafter Bateman, in view of Stevens.

Bateman discloses a liquid chromatograph mass spectrometer system in which a tandem quadrupole time-of-flight (Q-TOF) mass spectrometer has been programmed such that phosphorylated peptides can automatically be discovered and identified. Bateman discloses that alternate mass spectra, with and without fragmentation, are recorded at high and low collision energy. Bateman discloses that the method of the analysis is both compatible with and dependant on liquid chromatography for separation of complex mixtures. The method also incorporates acquisition of the product ion spectrum from any candidate precursor ions, thereby allowing confirmation of the neutral loss or product ion (abstract). Bateman discloses that the number of product ion spectra to be recorded may be further reduced by first testing to determine

whether or not the characteristic product ion or neutral loss is present. Bateman discloses that this is accomplished by operating the quadruple mass filter in the RF-only mode such as to simultaneously transmit a decade in mass into the gas collision cell with higher collision energy, sufficient to induce fragmentation. All ions from the source with m/z values above the low mass cut-off value, 0.78 times the set m/z value, of the RF-only quadrupole are transported through the quadrupole and fragmented in the gas collision cell. The orthogonal TOF mass spectrometer then records the mass spectrum of the resulting mixture of precursor and fragment ions. Bateman further discloses that it is only necessary to switch to low collision energy to prevent fragmentation and hence to record the mass spectrum of precursor ions only. Bateman discloses that by alternating the collision energy, it is possible to alternate between recording the spectrum exhibiting the mixture of precursor ions and their fragment ions. The operating conditions are set such that alternated spectra are recorded under at least two distinct operating modes, such as one of low collision energy (no significant fragmentation), and a second mode of high collision energy (mostly all precursor ions fragmented) (page 794). Bateman discloses that if the two operating modes are suitably set, precursor and product ions may be readily distinguished (page 795, full document).

Bateman does not disclose an operation device for adding data.

Stevens teaches a chromatogram system with two detectors and a fraction collector (Fig. 1). Chromatogram data are added or subtracted to scale the data (lines 56-58, col. 4).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by the fragmented and unfragmented ionization detection in order to scale data in a two-detection scheme chromatograph such as taught by Stevens. It would have been obvious to

modify the JP device to include a fraction collector to collect desired fractions as taught by Stevens, under control of the detector signal as was known in the art.

Claims 1 and 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman in view of Windig.

Bateman has been discussed above.

Bateman does not disclose an operation device for adding data.

Windig teaches a method for data handling for an LC-MS system. A summation of particular data is plotted to obtain an enhanced chromatogram (lines 1-19, col. 4).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by the fragmented and unfragmented ionization detection in order to enhance chromatograms such as taught by Windig. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1 and 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman in view of Watanabe.

Bateman has been discussed above.

Bateman does not disclose an operation device for adding data.

Watanabe teaches a method for data handling for a chromatogram-MS system. A summation of particular data is plotted to obtain a chromatogram of all mass vs. time (columns 7 and 8, figs. 4-7a).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by fragmented and unfragmented detection in order to provide a cumulative

chromatogram as taught by Watanabe. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Claims 1 and 3-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bateman in view of Sacks.

Bateman has been discussed above.

Bateman does not disclose an operation device for adding data.

Sacks teaches a method for data handling for a chromatographic system. A summation of particular data of the multiple columns forms a single chromatogram from FID 16, and in this way the chromatographic time dimension can be used more efficiently (lines 9-47, col. 8).

It would have been obvious to modify Bateman to add the data from the chromatograms generated by the fragmented and unfragmented detection in order to provide a single chromatogram and thus allow the chromatogram time dimension to be used more efficiently such as taught by Sacks. It would have been obvious to provide a fraction collector to collect desired fractions under control of the detector signal as was known in the art.

Response to Arguments

With regards to the Priority issued raised with regard to the subject matter of current claim 6 not supported in the prior-filed application, Application No. 10/015,668, Examiner asserts that claim 6 will not be afforded the prior-filed application's filing date.

With regards to the second rejection of claims 1-6 under 35 USC 112, 2nd paragraph, Applicant argues that there is no requirement for a one-to-one relationship between the claimed elements and the elements of the disclosed embodiment. Examiner asserts that either the specification or the claims should be amended, so that the terminology used in the both the claims and the specification corresponds in a one-to-one relationship. At present, the claims and specification differ in the terminology used to define the various devices. Additionally, the specification contains instances (as previously discussed in the Office Action dated 04/17/07) where one term may be taken to read on more than one of the claimed elements. As such the claimed elements are indefinitely defined.

The rejection of claim 1 with respect to how the adding of data is being done and which data is added together is maintained as discussed above.

Applicant's arguments filed June 25th, 2007 have been fully considered but they are not persuasive.

With regards to claims 1-5 rejected under 35 USC 103(a) over JP06102251A (JP) in view of Stevens (4,762,617), and claims 1-6 rejected under 35 USC 103(a) over Bateman in view of Stevens, Applicant argues that timing involved in separating and collecting the eluted fractions in the Stevens patent is fundamentally different from that claimed. Examiner argues that the

disclosure to Stevens was for the disclosure to an operating device (analysis computer 50) for adding or subtracting chromatogram data (lines 56-58, col. 4). Examiner further argues that the timing with which the eluted fractions are separated and collected has not been claimed and such an argument is thereby not commensurate in scope with the claims.

With regard to claims 1-5 rejected under 35 USC 103(a) over JP in view of Windig (6,329,652), and claims 1-6 rejected under 35 USC 103(a) over Bateman in view of Windig, Applicant argues that Windig does not disclose a detector which, at the same time with the same sample can detect the different fractions, and that Windig also does not disclose the separation/collection timing. Examiner argues that Applicant's arguments are not commensurate in scope with the claims because such a detector and process limitation associated with the detector are not claimed, and a specific separation/collection timing is not claimed.

With regards to claims 1-5 rejected under 35 USC 103(a) over JP in view of Watanabe (6,444,979) and claims 1-6 rejected under 35 USC 103(a) over Bateman in view of Watanabe, Applicant argues that Watanabe does not disclose the separation/collection. It is unclear what separation/collection in the claims Applicant is referring to in this argument. Applicant's argument is unclear with respect to the cited art. Examiner further asserts that Windig was provided for disclosure to an operating device for adding chromatogram data and not for separation/collection.

With regards to claims 1-5 rejected under 35 USC 103(a) over JP in view of Sacks (5,205,845), and claims 1-6 rejected under 35 USC 103(a) over Bateman in view of Sacks, Applicant argues that collection of the different eluted fractions from the chromatograph column is not disclosed. It is unclear what Applicant is arguing. What is different in Sacks with respect

to the collection of the different eluted fraction from the column? Further, Applicant's arguments are not commensurate in scope with the claims. Additionally, Sacks was provided for disclosure to an operating device for adding chromatogram data.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Neil Turk whose telephone number is 571-272-8914. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NT

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